PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Emrick et al.	
Serial No: 10/643,015	Attorney Docket No. 7163
Filed: August 18, 2003	
For: PYRIDINE AND RELATED LIGAND COMPOUNDS, FUNCTIONALIZED NANOPARTICULATE COMPOSITES AND METHODS OF PREPARATION	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RULE 131 DECLARATION OF HABIB SKAFF

1. I, Habib Skaff, am a co-inventor with regard to the invention (the "Invention") disclosed and claimed in the above-entitled application (the "Application"). I make this declaration in support of the Application and, in particular, to antedate a reference cited against the Application.

2. The Invention claimed in the Application was completed before the effective date of application serial number 10/219,440 (*i.e.*, the Dubertret

reference). More specifically, the Invention was conceived and with due diligence reduced to practice prior to the effective date of the Dubertret reference.

3. This Declaration, and prior invention, is supported by copies of pertinent pages from my laboratory research notebook, entries to which I contemporaneously signed and dated and were witnessed by co-inventor, Todd S. Emrick. Date redacted copies of the aforementioned notebook pages are provided collectively as Exhibit A and incorporated herein by reference. These documents establish that the Invention was made at least as early as June 1, 2002, which is a date earlier than the effective date of the Dubertret reference.

I hereby declare that: All statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; that those statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code; and that willful false statements may jeopardize the validity of the Application or any patent issuing thereon.

Date 12/13/04

Habib Skaff

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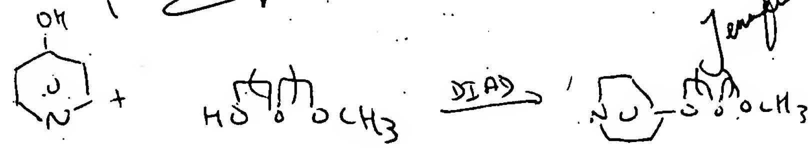
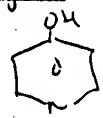


Reagents

95 ①  2g, 0.022 mol

750 ② m-Peg 750 14.25g, 0.019 mol

262 ③ Ph_3P 6.28g, 0.024 mol

202 ④ DIAD 4.84g, 0.024 mol (4.72 mL)

⑤ THF (dry) ~~300mL~~ 250 mL

Procedure

① Ph_3P + THF loaded into 2-neck flask & stirred under N_2 @ r.t.

② DIAD added via syringe & stirred for ½ hr.

③ "phenol" & alcohol added & stirred

④ reacted over night

⑤ rotavaped off THF

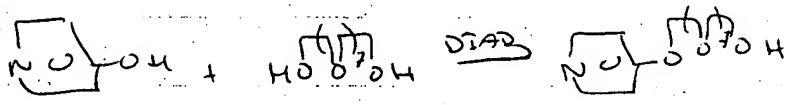
⑥ added H_2O & ether → washed w/ ether

⑦ extracted product out w/ CH_2Cl_2 out of ~~Aq~~ aq phase → $MgSO_4$, Rotavap

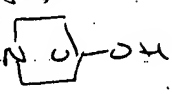
→ NMR show some  → tried redissolving in basic (.5M NaOH) solution & precipitating into CH_2Cl_2 (cold) — didn't work

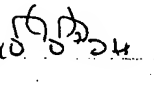
→ ran column eluting w/ CH_2Cl_2 : [illegible] : MeOH (7:3:0), (7:2:1)

Exhibit A



Reagents

95 ①  & 2g, 0.011mol

400 ρ=1.03 ②  22g, 0.055mol

202 ③ DIAD 2.63g, 2.55mL 0.013mol

262 ④ Ph_3P 3.41g, 0.013

⑤ THF(dry) 300mL

Procedure

① Ph_3P & THF loaded into 3-neck 500mL round bottom & stirred @ r.t. under N_2

② DIAD added via syr. & stirred for ½ hr.

③ phenol & ~~ethanol~~ added & stirred

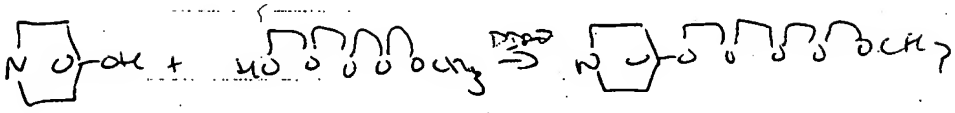
→ reacted overnight

- rotovaped off all THF → note

- extracted w/ H_2O → then aqueous washed w/ CH_2Cl_2 → too difficult to purify by column

→ rotovaped off CH_2Cl_2 → dissolved in H_2O, washed w/ ether, then Toluene → doesn't work well either

→ try ~~acidifying~~ acidifying aqueous to make pyridine salt which will not be soluble in



Reagents

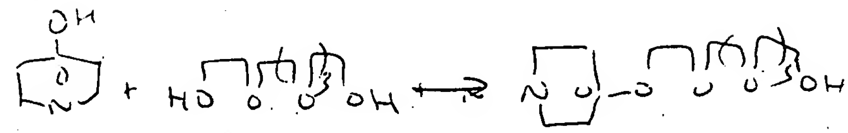
95	①	5g,	0.055 g/mol
128	② m-Tyr	5.632g,	0.044 mol
1.025 262	③ Ph_3P	13.1g	0.05 mol
202	④ DIAD	10.1g,	0.05 mol, 9.85 mL
	⑤ THF (dry)	~~75 mL~~	400 mL

Procedure

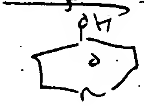
~~①~~ ④ Ph_3P & THF loaded into 2-neck flask & stirred under N_2 @ r.t.

② DIA added via syring & stirred for ½ hr.

③ phenol & alcohol added & stirred overnight



Reagents

95 ①  4g, 0.042mol

300 ② Heg 31.58g, 0.105mol

262 ③ Ph_3P 13.1g ~~0.045~~ 0.05mol

(=1.035) 202 ④ DIAD 10.1g, 0.05mol, ~~10.35mL~~ 9.85mL

⑤ THF 500mL

Procedure

① phenol, Ph_3P, DIAD, c̄ THF loaded in 2-neck & stirred @ r.t. under N_2 for ½ hr.

② diol added ⇒ stirred overnight

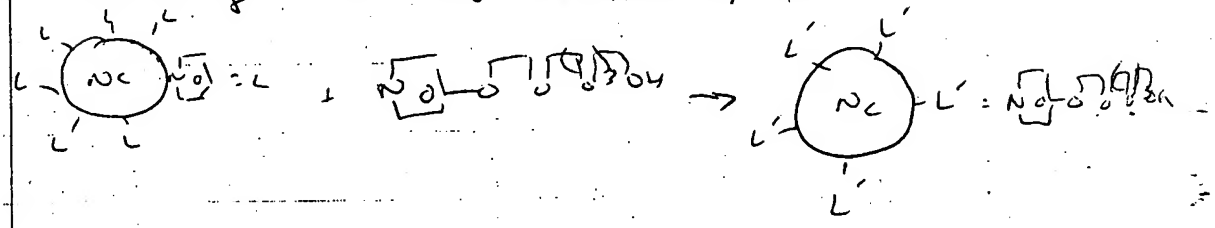
rotavaped off THF
⇒ first w/ $CHCl_3$ ② $CHCl_3$: [illegible] (80:20) ③ ~~CHCl~~ $CHCl_3$: [illegible]: MeOH (75:20:5)
run column eluting w/ ④ $CHCl_3$: [illegible]: MeOH (7:2:1)

tried distilling off unreacted diol @ ~~180~~ 224°C @ 600 mtorr ⇒ didn't work well

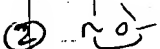
run column in $CHCl_3$: [illegible]: MeOH (78:20:2), (75:20:5), (80:20:10)

[signatures]

Exchange to peg-monopyridinyl ether



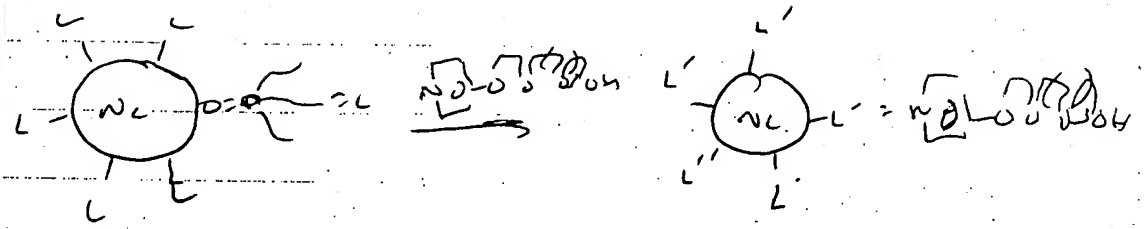
Reagent

① pyridine NC ~40mg
②  600mg
③ THF (dry) 3mL
④ DIW 6mL

Procedure

A ① 20mg NC dispersed in solution of 300mg new ligand in THF → immediately went into solution
② dried under N_2 flow and added 3mL DIW → most went into solution → centrifuged
B ② 20mg NC dispersed in solution of 300mg new ligand in 3mL DIW → NC went into solution → centrifuged

Jennifer L. Sneed



Reagents

1. TOPO covered NC ~15mg
2. [illegible] 320 mg
3. THF (dry) 3mL

Procedure

1. NC made as ~~exactly~~ usual & washed w/ MeOH 3 times
2. dried over N_2 flow
3. redissolved in new ligand in THF and allowed to stand over head of N_2 overnight
4. distilled at ½ THF → precipitated w/ hexane → all NC precipitated
5. washed w/ hexanes → centrifuged → redissolved in ~~DI~~ H_2O

[signature] [signature]

[signature] [signature]